

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Charles N. Serhan and
Bruce D. Levy

Application No.: Not yet assigned

Filed: Herewith

Entitled: SCREENING METHODS FOR
PRESQUALENE DIPHOSPHATE
ANALOGS

Group Art Unit: Pending

Examiner: Pending

BOX PATENT APPLICATION
Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Dear Sir:

Prior to examination, please amend the application as follows.

IN THE SPECIFICATION

On page 1, please replace the title with the following rewritten title:

- - SCREENING METHODS FOR PRESQUALENE DIPHOSPHATE ANALOGS- -

Please replace the paragraph on page 1, beginning at line 6 with the following rewritten paragraph:

- -This application is a continuation application of U.S. Application No. 09/793,005, filed

December 13, 2000 which is a continuation application of U.S. Application No. 09/539,591, filed March 31, 2000 which is a continuation application of U.S. Application No. 09/055,592, filed April 6, 1998 which is a continuation-in-part of U.S. Serial No. 08/832, 952, filed on April 4, 1997, the contents of which are hereby expressly incorporated by reference. - -

Please replace the paragraph on page 38, beginning at line 23 with the following rewritten paragraph:

- - IV.

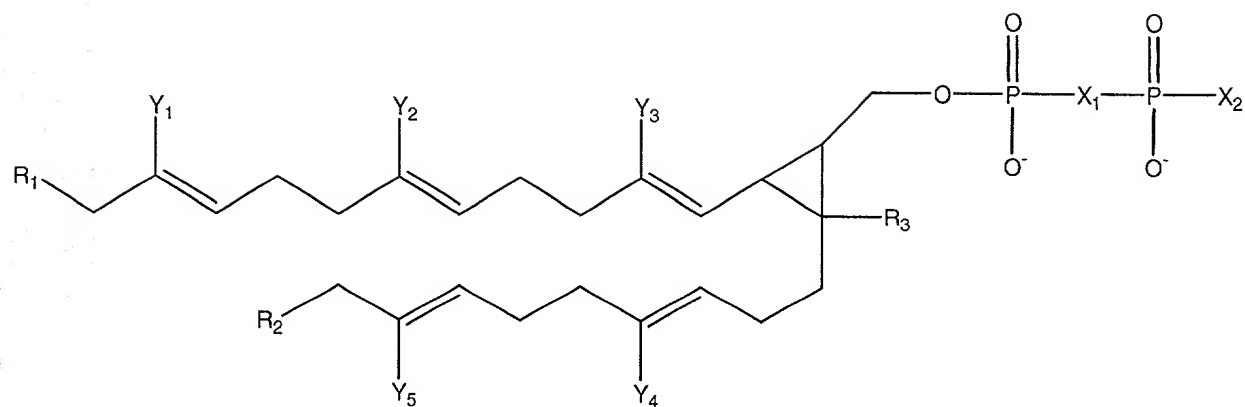
EXAMPLES - -

IN THE CLAIMS

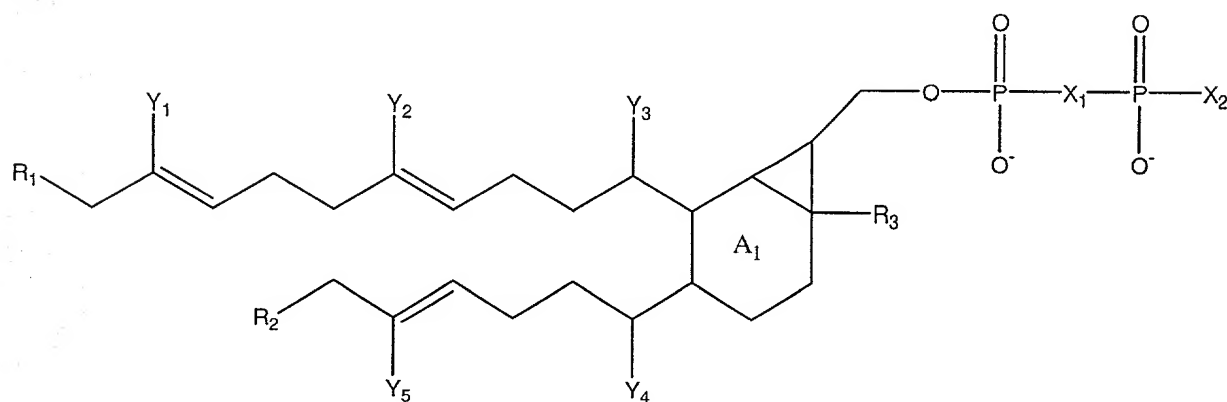
Cancel claims 2-31.

Add the following claims:

33. (New) A method for modulating generation of an active oxygen species in a subject, comprising administering to the subject an effective amount of farnesyl diphosphate, presqualene diphosphate, farnesyl monophosphate, presqualene monophosphate or a presqualene diphosphate analog.
34. (New) The method of claim 33, wherein the presqualene diphosphate analog is represented by one of the formulae (Formulas I and II):



(I)



(II)

wherein R_1 , R_2 and R_3 are each independently, a hydrogen atom, F, Cl, Br, I, CH_3 or substituted or unsubstituted, linear or branched alkyl, alkoxy, aryl, aralkyl or heteroaryl groups;

wherein Y_1 , Y_2 , Y_3 , Y_4 , and Y_5 are each independently hydrogen atoms or lower alkyl groups;

wherein X_1 is an oxygen atom, a sulfur atom, an $N=N$ group, a methylene or, NR_5 ,

wherein R_5 is a hydrogen atom or a substituted or unsubstituted, linear or branched alkyl, aryl,

aralkyl or heteroaryl group;

wherein X_2 is an OH group, SH, CH_3 , or NR_6R_7 , wherein R_6 and R_7 are each independently, a hydrogen atom or a substituted or unsubstituted, linear or branched alkyl, aryl, aralkyl or heteroaryl group; and

wherein A_1 is a nonaromatic carbocyclic group or a pharmaceutically acceptable salt thereof.

35. (New) The method of claim 34, wherein Y_1 , Y_2 , Y_3 , Y_4 and Y_5 are CH_3 , X_1 is $N=N$ and X_2 is OH.
36. (New) The method of claim 34, wherein Y_1 , Y_2 , Y_3 , Y_4 and Y_5 are CH_3 , X_1 is methylene and X_2 is OH.
37. (New) The method of claim 33, wherein the generation of the active oxygen species results from activation of leukocytes.
38. (New) The method of claim 37, wherein the activation is leukocyte migration.
39. (New) The method of claim 33, wherein the generation of the active oxygen species is associated with rheumatoid arthritis, asthma, or ARDS.
40. (New) The method of claim 33, wherein the generation of the active oxygen species is associated with physical trauma or radiation exposure.

REMARKS

Claims 1 and 33 through 40 are pending.

Support for new claims 33 through 40 can be found in the claims as originally filed in parent applications 08/832,952; 09/055,592; 09/539,591; and 09/736,005 and throughout the specification, more specifically at page 44, lines 11 through 25.

No new subject matter has been added.

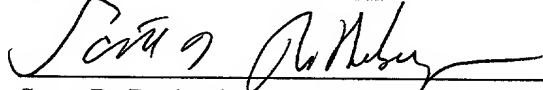
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Marked-up Version Showing Changes.**"

CONCLUSION

In view of the amendment and remarks, it is believed that this application is in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (612) 340-8819.

Respectfully submitted,

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Dated: 2/27/02

MARKED-UP VERSION SHOWING CHANGES

IN THE SPECIFICATION

On page 1, the title has been amended as follows:

[COMPOSITIONS AND] SCREENING METHODS FOR [NEUTROPHIL
RESPONSES] PRESQUALENE DIPHOSPHATE ANALOGS

Paragraph beginning on page 1, line 6 has been amended as follows:

This application is a continuation application of U.S. Application No. 09/539,591, filed March 31, 2000 which is a continuation application of U.S. Application No. 09/793,005, filed December 13, 2000 which is a continuation application of U.S. Application No. 09/055,592, filed April 6, 1998 which is a continuation-in-part of U.S. Application No. 08/832,952, [entitled "Novel Polyisoprenyl Phosphate Stable Analogs For Regulation of Neutrophil Responses"], filed April 4, 1997, the contents of which are hereby expressly incorporated by reference.

Paragraph beginning on page 38, line 23 has been amended as follows:

IV. *[Exemplification]* **EXAMPLES**

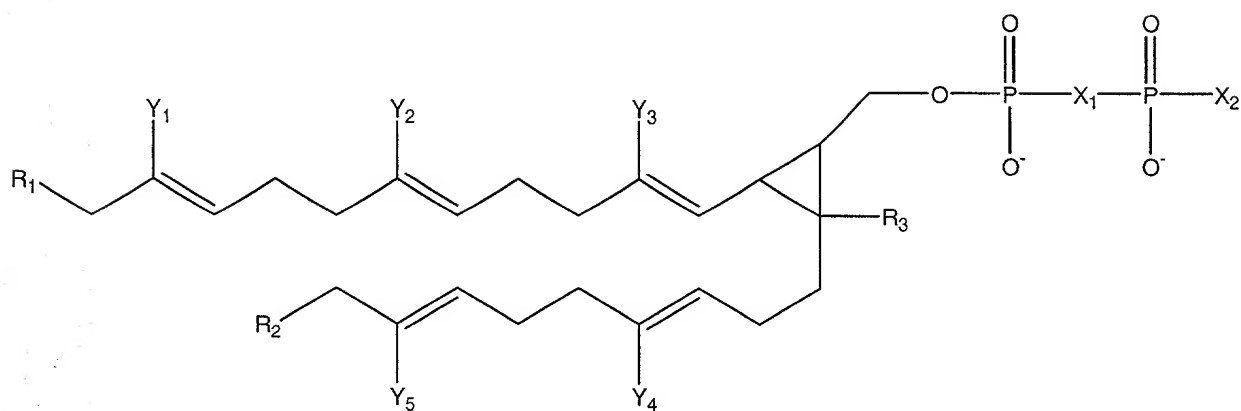
IN THE CLAIMS

Cancel claims 2-31.

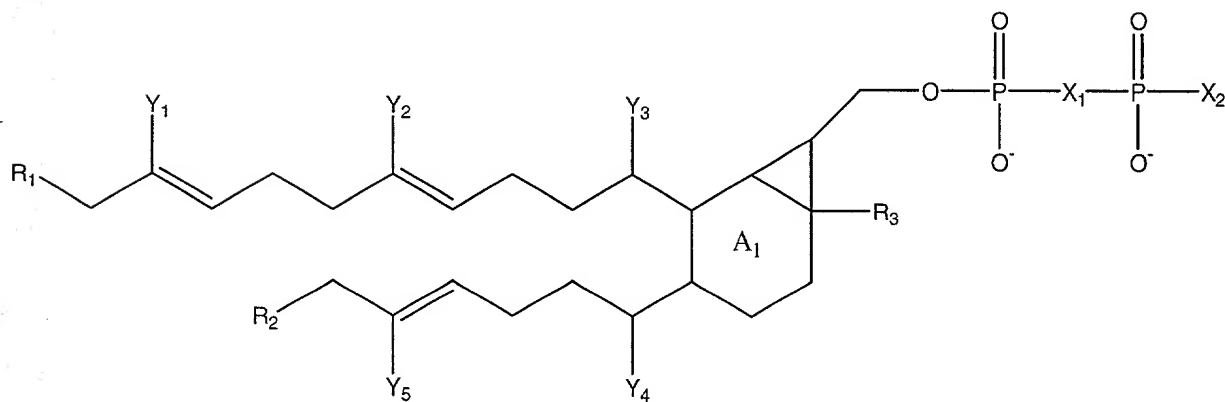
Add the following new claims:

33. (New) A method for modulating generation of an active oxygen species in a subject, comprising administering to the subject an effective amount of farnesyl diphosphate, presqualene diphosphate, farnesyl monophosphate, presqualene monophosphate or a presqualene diphosphate analog.

34. (New) The method of claim 33, wherein the presqualene diphosphate analog is represented by one of the formulae (Formulas I and II):



(I)



(II)

wherein R_1 , R_2 and R_3 are each independently, a hydrogen atom, F, Cl, Br, I, CH_3 or substituted or unsubstituted, linear or branched alkyl, alkoxy, aryl, aralkyl or heteroaryl groups;

wherein Y_1 , Y_2 , Y_3 , Y_4 , and Y_5 are each independently hydrogen atoms or lower alkyl groups;

wherein X_1 is an oxygen atom, a sulfur atom, an N=N group, a methylene or, NR_5 , wherein R_5 is a hydrogen atom or a substituted or unsubstituted, linear or branched alkyl, aryl, aralkyl or heteroaryl group;

wherein X_2 is an OH group, SH, CH_3 , or NR_6R_7 , wherein R_6 and R_7 are each independently, a hydrogen atom or a substituted or unsubstituted, linear or branched alkyl, aryl, aralkyl or heteroaryl group; and

wherein A_1 is a nonaromatic carbocyclic group or a pharmaceutically acceptable salt thereof.

35. (New) The method of claim 34, wherein Y_1 , Y_2 , Y_3 , Y_4 and Y_5 are CH_3 , X_1 is N=N and X_2 is OH.
36. (New) The method of claim 34, wherein Y_1 , Y_2 , Y_3 , Y_4 and Y_5 are CH_3 , X_1 is methylene and X_2 is OH.
37. (New) The method of claim 33, wherein the generation of the active oxygen species results from activation of leukocytes.
38. (New) The method of claim 37, wherein the activation is leukocyte migration.

39. (New) The method of claim 33, wherein the generation of the active oxygen species is associated with rheumatoid arthritis, asthma, or ARDS.
40. (New) The method of claim 33, wherein the generation of the active oxygen species is associated with physical trauma or radiation exposure.